

REMARKS

Figure 5 as originally filed as obvious errors in that ports 1 and 2 of the top valve of the column 101 should be labeled as ports 3 and 1, respectively. The description makes it clear that packing is effected via port 1 and excess liquid from packing is removed via port 3.

Specifically, the two valves at the top and bottom of the column as shown in the embodiment of Figure 5 are identical to those of Figures 3 and 4 and operate as described in the description of those Figures (see page 20, last line, to page 21, line 4). Packing can be achieved by introducing media using either the bottom or top valve when the chosen valve is in position of Figure 4, that is with the sleeve 24 retracted. The slurried media is pumped into the column via port 1. The media is retained in the column while forming the slurry vented through port 2 and the liquid forming the slurry then exits via port 3 (see page 16, lines 11-17).

Unpacking can be similarly achieved by either valve by, as described at page 18, lines 10-13, introducing reslurrying liquid via port 1 of the chosen valve and removing the reslurried media via port 2 of the valve.

Accordingly, it is clear from the description in relation to the general operation of the chromatography apparatus that:

- a) slurried media or reslurrying liquid is introduced via port 1;
- b) reslurried media is removed via port 2;
- c) excess liquid during packing is removed via port 3.

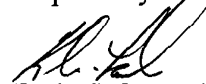
Finally, it is clear from the description (page 7, second full paragraph) that according to the first aspect of the invention, excess liquid (from port 3 during packing, step c) above) is not removed from the system (as in the prior art methods) but is returned to the slurry vessel.

The operation of the valves of the column 101 of Figure 5 is said to be as described in relation

to the other Figures (as set out above)(see page 20, last line and following), but it can be seen that Figure 5 as originally filed is obviously incorrect in the ports and their connections.

The foregoing amendment therefore corrects Figure 5 by labeling column 101 as having 3-port valves; by showing that the excess liquid obtained during packing exits port 3 and is returned to the slurry vessel via pipe 130; and by showing that the slurry pump 110 can feed slurry to port 1 of either column valve (selected by 3-way valve 114), so pipe 132 is now shown connected to port 1 of the top valve, and the separate connections of pipe 118 and 120 to ports 1 and 2 of the lower valve are now explicitly shown.

Respectfully submitted,



Kevin S. Lemack

Reg. No. 32,579

176 E. Main Street - Suite 8

Westboro, Massachusetts 01581

TEL: (508) 898-1818

system 100 includes a chromatography column 101 as previously described with reference to Figures 1, 3 and 4 and including top and bottom a valve as shown in Figures 3 and 4 of which ports 1 and 2 are referenced.

A slurry vessel 102 is partially filled with a slurry 104. An output pipe 106 from the bottom of the slurry vessel 102 leads to a T-junction 108 and hence as an input to a packing pump 110 and to a 3-port valve 112 via pipe 113.

The output of the packing pump 110 is coupled to a 3-port valve 114 by a pipe 116 and from there to ^{port 1 of the valve at} the base of the chromatography column 101 by a pipe 118. The 3-port valve 112 is also coupled to a pipe 120 which ~~joins the pipe 118 as so also leads to~~ ^{is coupled to port 2 of the valve} the bottom of the chromatography column 101 and by a pipe 122 to a circulating pump 124 whose output is coupled to a pipe 126 and hence to the slurry vessel 102 via a pipe 128.

Upper port ~~X~~³ of the chromatography column 101 is coupled to pipe 128 by a pipe 130. Upper port ~~X~~¹ of the chromatography column 101 is coupled to the 3-way valve 114 by a pipe 132.

The chromatography system 100 operates as follows. As a first, optional phase, the suspension 104 containing a fluid mixture including a target molecule and the chromatography media are introduced into the slurry vessel

to be noted the slurry concentration is maintained constant throughout the packing procedure. The method of the present invention, which ensures that all media particles with the adsorbed molecule are packed within the column, is as follows.

Upper port $\frac{3}{4}$ is opened during packing so the excess fluid is returned to the slurry vessel 102 via pipes 130 and 128 rather than being taken to a waste vessel for other storage vessel. This acts to dilute the media particles in the slurry 104 as packing progresses until all the particles have been retained within the column.

Chromatography media can be gradually added to the vessel until the column is packed thereby minimising the amount of media used to obtain a packed column. The return of the excess fluid to the vessel 102 also assists in the prevention of sedimentation of the slurry during the packing procedure.

Some of the advantages of embodiments of the system and method of the present invention can be summarised as follows:

- a) Batch contact between the chromatography media and the target molecule is achieved by the use of the fluid recycle loop, providing continuous agitation in a low shear environment and without the use of mechanical electrically driven

Replacement Sheet

Page 21, second full paragraph:

A¹
The output of the packing pump 110 is coupled to a 3-port valve 114 by a pipe 116 and from there to port 1 of the valve at the base of the chromatography column 101 by a pipe 118. The 3-port valve 112 is also coupled to a pipe 120 which is coupled to port 2 of the valve at the bottom of the chromatography column 101 and by a pipe 122 to a circulating pump 124 whose output is coupled to a pipe 126 and hence to the slurry vessel 102 via a pipe 128.

Page 21, third full paragraph:

A²
Upper port 3 of the chromatography column 101 is coupled to a pipe 128 by a pipe 130. Upper port 1 of the chromatography column 101 is coupled to the 3-way valve 114 by a pipe 132.

Page 23, first full paragraph:

A³
Upper port 3 is opened during packing so the excess fluid is returned to the slurry vessel 102 via pipes 130 and 128 rather than being taken to a waste vessel for other storage vessel. This acts to dilute the media particles in the slurry 104 as packing progresses until all the particles have been retained within the column.